REMARKS

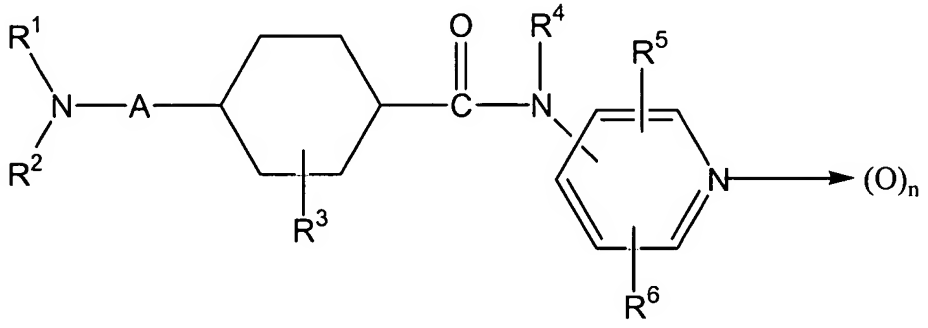
Status of the claims

Claims 1-9 and 11-22 are pending and claim 22 is under consideration in this application, claims 1-9 and 11-21 having been withdrawn from consideration on the grounds that they are drawn to a separate inventions. Claim 22 stands rejected. After entry of the amendments made herein, claims 1-9 and 11-33 will be pending and claims 22-33 will be under consideration, claims 23-33 having been added.

New claims 23-33 are supported by the specification. For the convenience of the Examiner, these newly added claims are repeated below and examples of textual support in the original claims and/or the specification (paragraph numbers from U.S. Patent Application Publication No.20020119140 (the '140 application)) are provided in parentheses after relevant embodiments.

23. (New) A method of stimulating regenerative growth (e.g., paragraphs 0013, 0037, 0067, and 0115) of damaged neuronal axons in a patient with traumatic nervous system damage, (e.g., paragraph 0067) the method comprising delivering directly at a traumatic lesion site (e.g., paragraph 0118) in a nerve in a patient, in an amount effective to suppress inhibition of neuronal axon growth (e.g., paragraphs 0042 and 0052), a Rho family antagonist that is:

(i) a compound with the structure



wherein

R^1 and R^2 are the same or different and respectively represent: hydrogen, C_{1-10} alkyl, C_{2-5} alkoxy-carbonyl, amidino, C_{3-7} cycloalkyl, C_{3-7} cycloalkylcarbonyl, or substituted or unsubstituted phenyl, phenylalkyl, bezoyl, naphthoyl, phenylalkoxy carbonyl, pyridylcarbonyl, or piperidyl, the substituent being selected from the group consisting of a halogen, C_{1-4} alkyl, C_{1-4} alkoxy, phenylalkyl, nitro, and amino,

R^1 and R^2 together form unsubstituted or substituted benzylidene, pyrrolidylidene, or piperidylidene, the substituent being selected from the group consisting of a halogen, C_{1-4} alkyl, C_{1-4} alkoxy, phenylalkyl, nitro, and amino,

R^1 or R^2 together with the adjacent nitrogen atom form pyrrolidinyl, piperidino, piperazinyl, morpholino, thiomorpholino, or pthalimido,

R^3 represents hydrogen or C_{1-4} alkyl,

R^4 represents hydrogen or C_{1-4} alkyl,

R^5 represents hydrogen, hydroxy, or C_{1-4} alkyl, or phenyloxy,

R^6 represents hydrogen or C_{1-4} alkyl,

A represents single bond, C_{1-5} straight chain alkylene, or alkylene that is substituted by C_{1-4} alkyl, and

n represents 0 to 1, or

(ii) an optical isomer of the compound or a pharmaceutically acceptable acid addition salt of the compound, (e.g., paragraph 0021 and claim 1 of the '348 patent)

wherein the antagonist stimulates regenerative growth of damaged neuronal axons past the lesion site, (e.g., paragraph 0121) and

wherein the antagonist has the ability, when triturated into primary retinal ganglion cells *in vitro*, to produce outgrowth of retinal ganglion cell neurites, the retinal ganglion cells being plated on a growth inhibitory substrate selected from the group consisting of myelin and chondroitin sulfate proteoglycan. (e.g., paragraphs 0034, 0115, and 0116)

24. (New) The method of claim 23, wherein the antagonist is Y27632. (e.g., original claim 10 and paragraphs 0012, 0021, 0034 to 0036, 0040, 0115, 0116, 0118, 0121, 0123, and 0124)

25. (New) The method of claim 23, wherein the nerve is a nerve in the central nervous system. (e.g., original claims 5 and 10 and paragraphs 0002, 0038, 0052, and 0067)

26. (New) The method of claim 23, wherein the nerve is a spinal nerve. (e.g., paragraph 0121)

27. (New) The method of claim 23, wherein the lesion site comprises a site of surgical injury. (e.g., paragraph 0121)

28. (New) The method of claim 23, wherein the regenerative growth comprises a twisted path of growth past the lesion site. (e.g., paragraph 0121)

29. (New) The method of claim 23, wherein the regenerative axon growth extends distal to the lesion site. (e.g., paragraph 0121)

30. (New) The method of claim 23, wherein the regenerative axon growth is up to 3 millimeter (mm) past the lesion site. (e.g., paragraph 0121)

31. (New) The method of claim 23, wherein the nervous system damage is selected from the group consisting of a spinal cord injury, a spinal cord lesion, and a surgical nerve lesion. (e.g., paragraphs 0035, 0052, and 0067)

32. (New) The method of claim 23, wherein the antagonist is administered with a pharmaceutical carrier or delivery system. (e.g., paragraphs 0052 and 0068)

33. (New) The method of claim 32, wherein the carrier is a fibrin adhesive. (e.g., paragraph 0121).

No new matter is added by any of the amendments made herein.

35 U.S.C. §112, first paragraph, rejections

(a) Claim 22 stands rejected on the grounds that the claims contain subject matter that was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

From the comments on page 2, line 15, to page 4, line 8, of the Office Action, Applicants understand the Examiner's position to be that genus encompassed by the term "a related compound" is not supported by adequate written description in the specification. Applicants respectfully disagree with this position in that the specification refers to a U.S. patent (No. 4,997,834; the '834 patent) as well as two scientific articles (Somiyo, 1997, Nature, 389:908-910; Uehata et al. Nature 389:990-994) that describe the family of compounds of which Y-27632 is member (see, e.g., paragraphs 0021 and 0040 of the '140 application). The Uehata et al. mentioned above provides the systematic name for Y-27632, i.e., (R)-(+)- *trans*-N-(4-pyridyl)-4-(1-aminoethyl)-cyclohexanecarboxamide (e.g., at page 993).

Notwithstanding these considerations, in order to expedite prosecution of the instant application, Applicants have deleted the term "or a related compound" from claim 22 and respectfully submit that the rejection is thus moot.

In addition, Applicants have added new claim 23 (and claims 24-33 that depend from claim 23) that, in addition to reciting a functional embodiments of the specified family of Rho antagonists lists the compounds described in the '834 patent (see, for example, claim 1 of the '834 patent). As is required for incorporation by reference, the instant specification makes it abundantly clear that the part of the'834 patent describing the family of compounds useful for the instant invention is "part of the referencing document as if it were fully set out therein." *In re*

Lund, 376 F.2d 982, 989 (CCPA 1967) Thus, for example, paragraph 0021 of the '140 application states in relevant part:

> Thus, compounds such as Y-27632 (U.S. Patent No. 4,997,834) that block Rho-associated kinase activity, thereby inactivating the Rho signaling pathway, are also embodiments of this invention. Thus, the use of other compounds within this family of compounds as described in U.S. Patent No. 4,997, 834 that inhibit Rho kinase are also considered within the scope of this invention.

In addition, paragraph 0040 of the '140 application states in relevant part:

> Preferred antagonists include . . . compounds such as Y-27632 that antagonize Rho-associated kinase (Somiyo, 1997, Nature, 389:908-910; Uehata, et al. Nature 389:990-994; U.S. Pat. No. 4,997,834)

(b) Claim 22 stands rejected on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

From the comments on page 4, line 9, to page 5, line 20, of the Office Action, Applicants understand the Examiner's position to be that the specification does not provide adequate enablement for the class of compounds referred to as "related compounds" in claim 22. While not agreeing with this position, Applicants submit that the above-described amendment to claim 22 renders the rejection moot.

35 U.S.C. §112, second paragraph, rejection

Claim 22 stands rejected on the grounds that it is allegedly indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

From the comments on page 6, lines 5-12, of the Office Action, Applicants understand the Examiner's position to be that term "related compounds" is indefinite. Applicants disagree with this position and, moreover, respectfully submit that, in light of the deletion of the term from claim 22, the rejection is moot.

35 U.S.C. § 102(b) rejections

Claim 22 stands rejected as allegedly being anticipated by Sylvain et al. (as evidenced by Eberlin et al.) and Varon et al. (as evidenced by Takahashi et al.).

From the comments on page 6, line 23, to page 9, line 5, of the Office Action, Applicants understand the Examiner's position to be that lovastatin (as disclosed in Sylvain et al.) and nerve growth factor (as disclosed in Varon et al.) are compounds related to Y-27632 and therefore claim 22 is anticipated by the two references. Applicants disagree with this position and respectfully submit that neither of these compounds could be construed as being related to Y-27632, especially given the teachings of the instant specification (e.g., those quoted above), including the references to the '348 patent. Moreover, in light of the above-described amendment to claim 22, Applicants submit that the rejections are moot.

CONCLUSION

In summary, for the reasons set forth above, Applicants maintain that the pending claims patentably define the invention. Applicants request that the Examiner reconsider the rejections as set forth in the Office Action, and permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' undersigned representative can be reached at the telephone number listed below.

Enclosed is a request for an automatic extension of time and a check in payment of the extension in time. Please charge any other fees or make any credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 12552-003001.

Respectfully submitted,

Date: 6/17/04

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